UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,366	12/05/2001	C. Frank Bennett	RTS-0332	1680

7590 09/24/2004

Jane Massey Licata
Licata & Tyrrell, P.C.
66 East Main Street
Marlton, NJ 08053

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,366	BENNETT ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-20* is/are pending in the application.

4a) Of the above claim(s) *15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-14,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-25-03, 11-25-01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence alignment data*.

DETAILED ACTION

This Office action is in response to the communication filed 7-12-04.

Claims 1, 2, 4-20 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2, 4-14, 19 and 20 in the reply filed on 7-12-04 is acknowledged. The traversal is on the ground(s) that no serious burden is presented to the examiner for searching the two distinct inventions. This is not found persuasive because the search required for the nucleic acids of Group I and the method of inhibiting expression of C2TA and treating diseases or conditions associated with the expression of C2TA, including treating autoimmune diseases using the nucleic acids, are not coextensive. Group I encompasses molecules that are claimed in terms of specifically hybridizing language (e.g. includes molecules with 80% identity to the target sequence) and the search for Group I would not necessarily be applicable to the method of using the nucleic acids claimed in Group I. Moreover, even if the nucleic acids claimed in Group I were known, the method of treatment which uses them may be novel and unobvious in view of the preamble or active steps.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7-12-04.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejections are governed by 37 CFR 1.116; amendments submitted after allowances are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to antisense oligonucleotides that specifically target and inhibit the expression of variants of MHC class II transactivator (MHC2TA) of SEQ ID NO: 3. The specification and claims do not adequately describe elements that are essential to the broad genus comprising variants of MHC2TA of SEQ ID NO: 3. The scope includes numerous structural variants and the genus is highly variant because it encompasses a large array of molecules. The specification teaches nucleotide sequences of some structural variants of human MHC2TA of SEQ ID NO: 3, including human MHC2TA-II, -III, -IV, -V, and –VI (see table 2, pages 93-97 of the instant disclosure). But these sequences represent only a subset of the broad genus

comprising variants of MHC2TA of SEQ ID NO: 3 (*see e.g.* Patarroyo et al, Genes and Immunity, 3(1): 34-37, text and table 1 on p. 34, figure 1 on p. 35, figure 2 on p. 35 for examples of human MHC2TA sequence variants obtained from screening the DNA from a sampling of normal Caucasians). Concise structural features distinguishing structures within the from others is missing from the claims and the disclosure. The specification fails to teach or adequately describe a representative number of species of the genus comprising variants of MHC2TA of SEQ ID NO: 3. Because the genus is so highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 11, 12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ting et al.

Ting et al (USPN 6,022,741) teach a composition comprising an antisense oligonucleotide between 8-50 nucleobases in length that specifically hybridizes to at least an 8 nucleobase portion of an active site on, and inhibits the expression of human MHC2TA of SEQ ID NO: 3, and which composition further comprises a

pharmaceutically acceptable diluent (e.g. water) (see alignment data for SEQ ID NO: 3 and col. 8, lines 5-21 of Ting et al).

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 11, 12, 14, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ting et al.

Ting et al (USPN 5,994,505) teach a composition comprising an antisense oligonucleotide between 8-50 nucleobases in length that specifically hybridizes to at least an 8 nucleobase portion of an active site on, and inhibits the expression of, human MHC2TA of SEQ ID NO: 3 (which comprises a variant of MHC class II transactivator), and which composition further comprises a pharmaceutically acceptable diluent (e.g. water) (see SEQ ID Nos: 4, 6, 7 and 8, and the accompanying sequence alignment

data, from Ting et al). It is noted that the instant specification as filed states that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid to be "specifically hybridizable (see pages 16-17 of the instant specification, especially page 16, lines 17-22). Based on the breadth of "specifically hybridize," these oligonucleotides would meet the structural limitations of the claimed oligonucleotides, because the oligonucleotide is within the size range of 8-50 nucleobases and is greater than 80% complementary to the nucleic acid of SEQ ID NO: 3 and would hybridize to such. Accordingly, the oligonucleotidea disclosed by Ting et al would specifically hybridize as claimed. The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression as claimed falls to applicant. See (In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 USC 102, on 'prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced b the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing In re Fitzgerald 205 USPQ 594, 596 (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to

Applicant to determine and provide evidence that the oligonucleotide disclosed by Ting et al would or would not have the additional "functional limitation" of specifically inhibiting expression of SEQ ID NO: 3, a variant of MHC class II transactivator, relative to the remaining variants of MHC2TA.

Therefore, absent evidence to the contrary, claims 1, 2, 11, 12, 14, 19 and 20 are anticipated by or, in the alternative, obvious over Ting et al.

Claims 1, 2, 11, 12, 14, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fabre et al.

Fabre et al (WO 98/15626) teach a composition comprising an antisense oligonucleotide between 8-50 nucleobases in length that specifically hybridizes to at least an 8 nucleobase portion of an active site on, and inhibits the expression of, human MHC2TA of SEQ ID NO: 3 (which comprises a variant of MHC class II transactivator), and which composition further comprises a pharmaceutically acceptable diluent (e.g. water) (see abstract, page 8, line 17 – page 9, line 24, claims 16-18). It is noted that the instant specification as filed states that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid to be "specifically hybridizable (see pages 16-17 of the instant specification, especially page 16, lines 17-22). Based on the breadth of "specifically hybridize," these oligonucleotides would meet the structural limitations of the claimed oligonucleotides, because the oligonucleotide is within the size range of 8-50 nucleobases and is greater than 80% complementary to the nucleic acid of SEQ ID NO: 3 and would hybridize to such. Accordingly, the

oligonucleotidea disclosed by Fabre et al would specifically hybridize as claimed. The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression as claimed falls to applicant. See (In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 USC 102, on 'prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced b the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing In re Fitzgerald 205 USPQ 594, 596 (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the oligonucleotide disclosed by Fabre et al would or would not have the additional functional limitation of specifically inhibiting expression of SEQ ID NO: 3, a variant of MHC class II transactivator, relative to the remaining variants of MHC2TA.

Therefore, absent evidence to the contrary, claims 1, 2, 11, 12, 14, 19 and 20 are anticipated by or, in the alternative, obvious over Fabre et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2 and 4-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ting et al, Ting et al or Fabre et al as applied to claims 1, 2, 11, 12 and 14 above, and further in view of McKay et al.

The claims are drawn to a composition comprising an antisense oligonucleotide between 8-50 nucleobases in length that specifically hybridizes to at least an 8 nucleobase portion of an active site on, and inhibits the expression of, human MHC2TA of SEQ ID NO: 3, which composition further comprises a pharmaceutically acceptable diluent (e.g. water) and a colloidal dispersion system, and which antisense oligonucleotide further comprises a phosphorothioate internucleotide modification, a 2'-

O-methoxyethyl modified sugar moiety, and a 5'-methylcytosine modified nucleobase, and which antisense is optionally chimeric.

Ting et al (USPN 5,994,505), Ting et al (USPN 6,022,741) and Fabre et al (WO 98/15626) are relied upon as cited in the rejections above.

The primary references of Ting, Ting and Fabre et al do not teach the incorporation of internucleotide, nucleobase or sugar modifications into antisense oligonucleotides, nor do they teach chimeric antisense structures, nor compositions comprising a colloidal dispersion system.

McKay et al (USPN 6,133,246, filed 4-7-1999) teach the incorporation of phosphorothioate internucleotide, 2'-O-methoxyethyl sugar and 5'-methyl cytosine modified antisense, as well as chimeric oligonucleotides and compositions comprising colloidal dispersion systems (see col. 7, line 63-col. 8, line 63, col. 10, lines 10-44col. 23, line 64- col. 24, line 67).

It would have been obvious to one of ordinary skill in the art to incorporate phosphorothioate, 2'-O-methoxyethyl sugar and 5-methyl cytosine modifications, as well as chimeric oligonucleotides, into antisense oligonucleotides because they were all well known in the art at the time the invention was made and one would have been motivated to incorporate these modifications into antisense oligonucleotides because McKay et al teach these modifications as well as chimeric antisense for increasing oligonucleotide stability, target binding and cellular uptake. One of ordinary skill in the art would have been motivated to use compositions comprising antisense and a colloidal dispersion system for transfections and target cell delivery of antisense in vitro

because McKay et al teach such systems for increasing cellular uptake of antisense. One of ordinary skill in the art would have expected that antisense oligonucleotides with the linkage, base and sugar modifications taught by McKay would have increased nuclease resistance, as well as enhanced target binding and cellular uptake. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ
9-17-04

TC1600